IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

AFFYMETRIX, INC.,   :
                                     :
          Plaintiff,   :
                                     :
     v.   :   Civil Action No. 04-901 JJF
                                     :
ILLUMINA, INC.,   :
                                     :
          Defendant.   :

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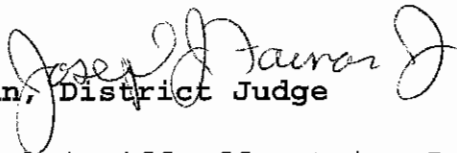
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MEMORANDUM OPINION

August 16, 2006
Wilmington, Delaware

Farnan, District Judge

Plaintiff Affymetrix, Inc. ("Affymetrix") filed this patent infringement action against Defendant Illumina, Inc. ("Illumina"). Affymetrix alleges that Illumina has infringed U.S. Patent Nos. 6,355,432 (the "'432 patent"), 6,646,243 (the "'243 patent), 5,545,531 (the "'531 patent"), 6,399,365 (the "'365 patent"), 5,795,716 (the "716 patent"). Presently before the Court is the claim construction dispute of the parties. The parties briefed their respective positions, and the Court held a <u>Markman</u> hearing on April 20, 2006. This Memorandum Opinion provides the Court's construction of the claim terms and phrases disputed by the parties.

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BACKGROUND

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The inventions claimed in the patents-in-suit relate to methods and apparatus for conducting analysis of unknown polymer sequences using microarrays of known polymer sequences and associated technology. Typically, these involve the detection and identification of sample nucleic acid sequences for use in genetic analysis. The parties have presented fifteen claim terms and phrases for the Court to construe. The Court will address each in turn.

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DISCUSSION

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I. Legal Principles Of Claim Construction

Claim construction is a question of law. <u>Markman v.</u>

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Westview Instruments, Inc., 52 F.3d 967, 977-78 (Fed. Cir. 1995),
aff'd, 517 U.S. 370, 388-90 (1996). In interpreting a claim, a
court should look first to the intrinsic evidence, i.e. the
patent itself, including the claims and the rest of the
specification, and, if in evidence, the prosecution history.
Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1582 (Fed.
Cir. 1996). Although it is within the sound discretion of a
court to use extrinsic evidence as an aid in construing a claim,
extrinsic evidence is "unlikely to result in a reliable
interpretation of patent claim scope unless considered in the
context of the intrinsic evidence." Phillips v. AWH Corp., 415
F.3d 1303, 1319 (Fed. Cir. 2005) (en banc).

A claim term should be construed to mean "what one of
ordinary skill in the art at the time of the invention would have
understood the term to mean." Markman, 52 F.3d at 986. However,
"the person of ordinary skill in the art is deemed to read the
claim term not only in the context of the particular claim in
which the disputed term appears, but in the context of the entire
patent, including the specification." Phillips, 415 F.3d at
1313. Thus, the specification is usually "dispositive; it is the
single best guide to the meaning of a disputed term." Id. at 1315
(quoting Vitronics, 90 F.3d at 1582). In other words, a claim
term can be given its correct construction only within the
context of "what the inventors actually invented and intended to

envelop with the claim."   <u>Phillips</u>, 415 F.3d at 1316.

II.   Construction Of The Disputed Terms

A.   The '432 Patent

The disputed phrase and term from the '432 patent are in claim 1 which claims: "A collection of beads comprising a plurality of beads which have binding polymers of different target specific sequence attached thereto; <u>said beads being coded with an encoding system</u> whereby the <u>target specific sequence</u> of the polymer attached to the beads can be identified."   ('432 patent, col. 82, ll. 51-54 (emphasis added).)

1.   Construction Of "Said Beads Being Coded With An Encoding System"

Affymetrix's proposed construction of "said beads being coded with an encoding system" is "said beads being distinguishable one bead from another."   (D.I. 243 at 10.) Illumina's proposed construction is "said beads having a property associated with each bead (separate from the binding polymer) that can be used to distinguish one bead from another."   (D.I. 240 at 16.)   The parties dispute only whether the Court should construe the term so as to preclude the use of the binding polymers themselves as the encoding system.   The Court concludes that it should.

The language of claim 1 and the specification indicates that the inventors did not contemplate using the binding polymers as the system to encode the beads to which they are attached.   Claim

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1 requires that the beads be "coded with an encoding system whereby the target specific sequence of the polymer attached to the beads can be identified." (Id. col. 82, ll. 53-55.) The specification teaches that "[a]fter the relatively small number of beads that have bound the target have been collected, the encoding scheme may be read off to determine the specificity of the reagent on the bead."[1] (Id. col. 21, ll. 58-61.) Thus, the patent teaches that the encoding system is used to identify which binding polymer is attached to a particular bead. Using the binding polymers as the encoding system then, would amount to using a binding polymer to identify itself. This circular identification cannot be what the inventors intended.

Affymetrix describes what it says is an example of a system using the polymers attached to the beads as both binding polymers and an encoding system. (D.I. 243 at 11-12.) However, what Affymetrix describes is not an encoding system per se, but a means of identifying the polymers attached to the beads by hybridizing them to known polymer sequences. To be useful, this system would still require a means of encoding the beads separate from the binding polymers. Subsequent to hybridization and identification of which polymer was attached to which bead, the beads would have to be encoded in some way, either by labeling

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[1]   In this context, the term "reagent," used in the specification, is synonymous with the term "binding polymer" used in the claims.

them directly or by recording their positions within an array of immobilized beads. Otherwise, the identifying information gained through hybridization with a known sequence would be lost when the known sequence was detached to free the binding polymer for further hybridization with an unknown target polymer.

Affymetrix also cites a section of the specification that it contends is a preferred embodiment teaching the use of the binding polymers as the encoding system. (D.I. 243 at 12; D.I. 250 at 10.) Affymetrix mischaracterizes the cited section. That section is a discussion of adding polymers to various products as markers to identify the origins of those products. It has nothing to do with using binding polymers as a system for encoding beads to which they are attached. (See '432 patent, col. 58, ll. 8-34.)

For the reasons discussed above, the Court construes "said beads being encoded with an encoding system" to mean "said beads having a property associated with each bead (separate from the binding polymer) that can be used to distinguish one bead from another."

2.   Construction Of "Target Specific Sequence"

Affymetrix's proposed construction of "target specific sequence" is "a known polymer sequence that has affinity for another sequence." (D.I. 243 at 13.) Illumina's proposed construction is "a known sequence of a polymer that binds with

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specificity to the target at the sequence to be determined."
(D.I. 240 at 18.)   The dispute here is whether the known polymer
sequence attached to a bead must have affinity merely for some
other sequence or whether the sequence for which it has an
affinity must be the sequence to be determined.   The Court
concludes that the attached polymer sequence must have an
affinity for some other sequence, not necessarily the sequence to
be determined.

The Court need look no further than the claim language to
conclude that Illumina's proposed construction is inappropriate.
The claim requires that each bead in the collection have attached
to it a polymer with a unique, known, target specific sequence.
Thus, for any given sequence to be determined, only one known
polymer sequence will bind with specificity to that sequence to
be determined.   Under Illumina's proposed construction,
therefore, only one bead in the collection would have a target
specific sequence attached to it.   This plainly contradicts the
claim language, which requires each bead to have an attached
target specific sequence.   A construction that produces an
unnecessary contradiction in the claim language cannot be
correct.   Therefore, the Court construes "target specific
sequence" to mean "a known polymer sequence that has affinity for
another sequence."

B.   The '243 Patent

The disputed terms from the '243 patent are in claim 14 which claims:

An apparatus for analyzing nucleic acid binding, comprising:

a substrate that comprises at least 1000 different spheres, beads, or particles having different species of nucleic acids attached thereto, the area of the substrate containing the at least 1000 spheres, beads, or particles being less than 1 cm2, at least some of the nucleic acids being bound to fluorescently labeled target nucleic acids;

a laser energy source to illuminate the fluorescent labels;

a detector to detect a fluorescent label bound to said target nucleic acids; and

a data collection system for storing fluoresced light intensity.

('243 patent, col. 30, ll. 53-67(emphasis added).)

1.   Construction Of "Substrate"

Affymetrix's proposed construction of "substrate" is "a material having a rigid or semi-rigid surface."   (D.I. 243 at 15.)   Illumina's proposed construction is "a material having a rigid or semi-rigid surface on which polymers are synthesized." (D.I. 240 at 8.)   Thus, the dispute here is whether the Court should construe "substrate" so as to limit the term to mean a surface on which polymers are synthesized.   The Court agrees with Affymetrix that no such limitation is required.

A patentee "is free to act as his own lexicographer, and may

set forth any special definitions of the claim terms in the
patent specification or file history, either expressly or
impliedly." Schoenhaus v. Genesco, Inc., 440 F.3d 1354, 1358
(Fed. Cir. 2006) (citing Irdeto Access, Inc. v. Echostar
Satellite Corp., 383 F.3d 1295, 1300 (Fed. Cir. 2004)). When a
specification reveals a special definition given to a claim term
by the patentee, "the inventor's lexicography governs." Phillips
v. AWH Corp., 415 F.3d 1303, 1316 (Fed. Cir. 2005). The
specification of the '243 patent includes a glossary section in
which "substrate" is expressly defined as "[a] material having a
rigid or semi-rigid surface." ('243 patent, col. 7, ll. 35-36.)
Moreover, that definition is consistent with the use of the term
"substrate" throughout the specification.

The glossary definition is followed by two sentences that
read:

> In many embodiments, at least one surface of the
> substrate will be substantially flat, although in some
> embodiments it may be desirable to physically separate
> synthesis regions for different polymers with, for
> example, wells, raised regions, etched trenches, or the
> like. According to other embodiments, small beads may
> be provided on the surface which may be released upon
> completion of synthesis.

(Id., col. 7, ll. 36-43.) Illumina contends that these sentences
are part of the express definition and should serve to limit that
definition to rigid and semi-rigid surfaces upon which polymers
are synthesized. (D.I. 240 at 8-9.) However, these explanatory
sentences are descriptive only of particular embodiments and the

Court will not import limitations from particular embodiments into the claims. See JVW Enterprises, Inc. v. Interact Accessories, Inc., 424 F.3d 1324, 1335 (Fed. Cir. 2005).

Illumina also contends that the Court should adopt Illumina's more narrow construction because, during prosecution of a parent application to the '243 patent,[2] Affymetrix distinguished a prior art reference "by arguing that this reference did not disclose how to synthesize sequences at known locations on a substrate, but instead taught how to attach pre-synthesized sequences." (D.I. 240 at 12.) "Where an applicant argues that a claim possesses a feature that the prior art does not possess in order to overcome a prior art rejection, the argument may serve to narrow the scope of otherwise broad claim language." Seachange Intern., Inc. v. C-COR, Inc., 413 F.3d 1361, 1373-74 (Fed. Cir. 2005) (citations omitted). Such a disclaimer must, however, be "clear and unmistakable." Omega Engineering, Inc. v. Raytek Corp., 334 F.3d 1314, 1325-26 (Fed. Cir. 2003). What Affymetrix actually disclaimed was that the invention claimed in the parent application could be practiced other than through in situ synthesis of sequences. The invention claimed in claim 14 of the '243 patent is very different from that invention, and, unlike the language of the parent

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[2]   Application number 07/492,462 which issued as U.S. Patent No. 5,143,854 (the "'854 patent").

application, the language of claim 14 does not expressly limit the invention to _in situ_ synthesis. Therefore, the Court cannot conclude that the statements made in the prosecution history of the parent application amount to a clear and unmistakable disclaimer with regard to the scope of claim 14 of the '243 patent. For the reasons discussed above, the court construes "substrate" to mean "a material having a rigid or semi-rigid surface."

2.   Construction Of "Target Nucleic Acids"

Affymetrix's proposed construction of "target nucleic acids" is "nucleic acids that have an affinity for the nucleic acid attached to the bead." (D.I. 243 at 18.) Illumina's proposed construction is "sample nucleic acids with sequence to be determined." (D.I. 240 at 12.)

The term "target nucleic acid" does not appear in the specification of the '243 patent. Affymetrix contends that the term is a synonym of the term "receptor," which is expressly defined in the '243 patent's glossary, and thus, the Court should adopt the glossary definition of "receptor" as its construction of "target nucleic acid." (D.I. 243 at 19-20.) However, it is not precisely correct to say that the two terms are synonymous. As Affymetrix recognizes, the set of "target nucleic acids" is a subset of "receptors," (_Id._ at 19.), so, while the terms are closely related, they are not synonymous. The construction of

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"target nucleic acids" must capture some meaning that
differentiates that subset from the broader set of "receptors."
Affymetrix's proposed construction does not do that and is thus,
too broad.

On the other hand, Illumina's proposed construction is too
narrow. Despite Illumina's references to particular examples and
embodiments, (see D.I. 240 at 13-14; D.I. 249 at 12-13), there is
nothing in the specification or in claim 14 that would limit the
"target nucleic acids" to those "with sequence to be determined."
While it is true that in some embodiments the purpose of exposing
the "target nucleic acids" to the nucleic acids attached to the
substrate is to determine the sequence of the target, (see, e.g.,
'243 patent, col. 10, ll. 3-24.), the Court will not import such
a limitation into the claim. See JVW Enterprises, 424 F.3d at
1335.

It is clear to the Court, from the claim language itself,
that the term "target nucleic acids" simply means nucleic acids
that are deliberately exposed to the nucleic acids attached to
the substrate. The Court construes the term accordingly.

   C.   The '531 Patent

The disputed term and phrase from the '532 patent are in
claim 1 which claims:

   A method for making a biological chip plate comprising
   the steps of:

(a) providing a body comprising a plurality of wells defining spaces;

(b) providing a wafer comprising on its surface a plurality of <u>probe arrays</u>, each <u>probe array</u> comprising a collection of probes, at least two of which are different, <u>arranged in a spacially defined and physically addressable manner</u>;

(c) attaching the wafer to the body so that the <u>probe arrays</u> are exposed to the spaces of the wells.

('531 patent, col. 12, ll. 40-51 (emphasis added).)

      1.   <u>Construction Of "Probe Array"</u>

Affymetrix's proposed construction of "probe array" is "a collection of surface-immobilized molecules, at least two of which are different, that can be recognized by a particular target." (D.I. 243 at 21.) Illumina's proposed construction is "a collection of probes, at least two of which are different, that are surface-immobilized (chemically linked) to a single surface." (D.I. 240 at 21.) The parties agree that the Court's construction should incorporate the express definitions of "probe" and "array" provided in the '531 patent's glossary. (D.I. 250 at 16; D.I. 240 at 21.) The parties' dispute is over Illumina's contention that the construction should be further limited to require that the molecules be attached via a chemical linkage and that they be attached to a single surface.

The term "probe array" is explicitly defined in claim 1 of the '531 patent: "each probe array comprising a collection of probes, at least two of which are different, arranged in a

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spacially defined and physically addressable manner . . . ."
('531 patent, col. 12, ll. 46-49.)   Furthermore, this definition
is identical to the '531 patent's glossary definition of "array."
(Id., col. 4, ll. 1-3.)   For the same reasons discussed in
section II.B.1. supra, the Court concludes that this definition,
chosen by the inventors acting as their own lexicographers,
governs here.

The further limitations Illumina seeks are not required.
Illumina contends that the language of claim 1 supports its
position that a "probe array" must be on a single surface.   The
language Illumina relies upon reads: "a wafer comprising on its
surface a plurality of probe arrays . . . ." (D.I. 240 at 21.)
However, while this language arguably might limit the wafer to a
single surface, it says nothing about the surfaces of the probe
arrays.

Illumina also points to various embodiments in support of
the claim limitations it urges. (Id. at 22-23.)   The Court
concludes that importation of limitations from those embodiments
into the claims would be improper. See JVW Enterprises, 424 F.3d
at 1335.

Finally, Illumina cites language from the prosecution
history. (D.I. 240 at 24.)   Like the claim language, however,
the cited language refers to the surface of the wafer, not the
surfaces of the probe arrays.   For the reasons discussed above,

the Court construes "probe array" to mean "a collection of probes, at least two of which are different, arranged in a spacially defined and physically addressable manner."

2.   Construction Of "Arranged In A Spacially Defined And Physically Addressable Manner"

Affymetrix's proposed construction of "arranged in a spacially defined and physically addressable manner" is "located in a particular location and capable of being addressed." (D.I. 243 at 23.) Illumina's proposed construction is "each probe in an array is placed in a different pre-determined location on the surface." (D.I. 240 at 24.) The dispute here is whether each probe's location within an array must be determined before it is attached to, or synthesized on the substrate. The Court concludes that neither the claim language nor the specification requires such a limitation.

Illumina cites six passages from the specification in support of its contention that each probe's location within an array must be pre-determined. (D.I. 240 at 25; D.I. 249 at 24-25.) Three of the cited passages, however, do not pertain to the arrangement of probes within an array, but to the arrangement of probe arrays on a wafer. (See '531 patent, col 2, ll. 64-7; col. 8, ll. 61-col. 9, l. 1; col. 11, ll. 58-64.) Furthermore, the other three passages, while pertinent to the arrangement of probes within an array, say nothing about when the probes' locations must be determined. (See Id., col. 1, ll. 15-16; col.

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10, ll. 36-44, 45-47.)   Therefore, the Court construes "arranged

in a spacially defined and physically addressable manner" to mean

"located in a particular location and capable of being

addressed."

D.   The '365 Patent

The disputed phrase and term from the '365 patent are in

claim 1, which claims:

A package from hybridization, comprising:

a substrate comprising a first surface including a
probe array with different probes comprising <u>biological
polymers immobilized on said first surface</u>; said probe
array including a density exceeding 100 different
biological polymers per cm2; and

a <u>housing</u> including a fluid cavity constructed and
arranged for hybridization of a target to a probe of
said probe array, said <u>housing</u> including a bar code.

('365 patent, col. 23, ll. 10-18 (emphasis added).)

1.   <u>Construction Of "Biological Polymers Immobilized On
A Surface"</u>

Affymetrix's proposed construction of "biological polymers

immobilized on a surface"[3] is "two or more surface-immobilized

biological polymers that are recognized by a particular target."

(D.I. 243 at 26.)   Illumina's proposed construction is "two or

more biological polymers of different sequence chemically linked

to a single surface."   (D.I. 240 at 28.)   The dispute here is

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[3]   Both parties agree that the various permutations of
this term in the '365 patent claims have the same meaning.   (D.I.
243 at 26; D.I. 240 at 28.)

whether the construction should be limited to require that the polymers be chemically attached, and that they be attached to a single surface. The Court concludes that these limitations are not required.

The claims require only that the biological polymers be immobilized; there is no claim language requiring that the immobilization be accomplished via a chemical linkage. In support of its proposed construction, Illumina cites one preferred embodiment in which the polymers are chemically linked to the substrate. (D.I. 240 at 28.) The Court will not import this limitation from that embodiment into the claims. See JVW Enterprises, 424 F.3d at 1335.

Illumina also contends that the language of both the claims and the specification requires that the polymers in the probe arrays be attached to a single surface. (D.I. 240 at 28-29.) Illumina's contention rests mainly on the fact that the claims and the specification refer to substrates or surfaces in the singular form, e.g. "a substrate," "a first substrate." (Id. at 29.) As Affymetrix points out, however, the Federal Circuit has held that "[u]nless the claim is specific as to the number of elements, the article 'a' receives a singular interpretation only in rare circumstances when the patentee evinces a clear intent to so limit the article." KCJ Corp. v. Kinetic Concepts, Inc., 223 F.3d 1351, 1356 (Fed. Cir. 2000). The Court finds no such intent

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here.

Moreover, Affymetrix points to three embodiments in which a probe array's substrate may comprise multiple surfaces. One of those embodiments is in the '365 patent itself and the other two are in the '854 patent, which is incorporated by reference in the '365 patent. (D.I. 243 at 27; D.I. 250 at 21 n.14.) Illumina's proposed construction would exclude these embodiments, and a claim construction that excludes a preferred embodiment "is rarely, if ever, correct and would require highly persuasive evidentiary support . . . ." Vitronics Corp. v. Conceptronic, Inc., 90 F.3d 1576, 1583 (Fed. Cir. 1996) (citations omitted). The Court finds no such support here. Therefore, the Court construes "biological polymers immobilized on a surface" to mean "two or more surface-immobilized biological polymers that are recognized by a particular target."

        2.   Construction Of "Housing"

Affymetrix's proposed construction of "housing" is "a structure in which something is contained." (D.I. 243 at 28.) Illumina's proposed construction is "casing that separates the probe array from the atmosphere." (D.I. 240 at 26.) The dispute here is over Illumina's contention that the construction of "housing" should require that the housing separate the probe array from the atmosphere. The Court concludes that such a limitation is not required.

The term "housing" appears in the '365 patent only in the claims and the abstract.   There is no language in the claims that would limit the term to require separation of the probe array from the atmosphere.   Thus, if such a limitation were warranted, it would have to come from the specification.   Illumina cites three passages from the specification in support of its proposed construction.   (D.I. 240 at 27; D.I. 249 at 26.)   None of the cited passages discusses separation of the probe array from the atmosphere.   One cited passage from the summary of the invention does mention "forming a sealed thermostatically controlled chamber in which fluids can easily be introduced . . . ." ('365 patent, col. 2, ll. 8-9.)   However, it is clear in context that the purpose of the seals is "to retain the fluid within the cavity" (Id., col. 2, l. 5),   not necessarily to separate the probe array from the atmosphere.

In support of its proposed construction, Affymetrix cites a definition of "housing" from Random House Webster's Unabridged Dictionary (1998).   The cited definition, "anything that covers or protects," differs from the proposed construction, "a structure in which something is contained."   The Court finds the cited definition closer to the meaning of "housing" as used in the specification than the proposed construction.   The American Heritage Dictionary's definition is similar, defining "housing" as "something that covers, protects, or supports . . . ." The

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American Heritage Dictionary of the English Language, Fourth

Edition (2000). As consistently described throughout the

specification, the "housing"[4] performs all three of the functions

listed in that definition. Therefore, the Court construes

"housing" to mean "a structure that covers, protects, and

supports the probe array."

     E.   The '716 Patent

     The disputed terms and phrases from the '716 patent are in

claim 1, which claims:

> A computer program product that identifies an unknown
> base in a sample nucleic acid sequence, comprising:
>
> computer code that receives a plurality of signals
> corresponding to probe intensities for a plurality of
> nucleic acid probes, each probe intensity indicating an
> extent of hybridization of a nucleic acid probe with at
> least one nucleic acid sequence including said sample
> sequence, and each nucleic acid probe differing from
> each other by at least a single base;
>
> computer code that performs a comparison of said
> plurality of probe intensities to each other;
>
> computer code that generates a base call identifying
> said unknown base according to results of said
> comparison and said sequences of said nucleic acid
> probes; and
>
> a computer readable medium that stores said computer
> codes.

('716 patent, col. 41, l. 60 - col. 42, l. 67 (emphasis added).)

     1.   Construction Of "Probe"

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     [4]   The Court considers the terms "body" and "casing,"
which are used throughout the specification, to be synonymous
with "housing" as used in the abstract and the claims.

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Affymetrix's proposed construction of "probe" is "a nucleic acid of known sequence that is capable of hybridizing to its complementary sequence." (D.I. 243 at 30.) Illumina's proposed construction is "a nucleic acid of known sequence that is capable of hybridizing to a complementary sequence of the unknown sample nucleic acid." (D.I. 240 at 30.) The Court concludes that Illumina's construction cannot be correct because it would exclude from the definition of "probe" some known nucleic acid sequences that the inventors clearly meant to encompass with the term.

As illustrated in one embodiment ('716 patent, col. 5, l. 44 - col. 6, l. 25), not all of the probes on a chip (i.e. in the "plurality of nucleic acid probes") need have a sequence complementary to a sequence of the sample nucleic acid. Those probes that do not are not "capable of hybridizing to a complementary sequence of the unknown sample nucleic acid." Therefore, some known sequences that the inventors clearly call probes would not fall within Illumina's proposed construction.

Illumina makes clear that its proposed construction differs from Affymetrix's in order to emphasize that the claims require hybridization of probes with the sample sequence. (D.I. 249 at 29.) As Affymetrix acknowledges (D.I. 243 at 31.), this is stated explicitly in the claims. Therefore, it need not be included in the construction of "probe." For the reasons

discussed above, the Court construes "probe" to mean "a nucleic acid of known sequence that is capable of hybridizing to its complementary sequence."

>   2.   Construction Of "Probe Intensity"

Affymetrix's proposed construction of "probe intensity" is "a detectable signal, e.g. fluorescence." (Id.) Illumina's proposed construction is "intensity from a labeled sample nucleic acid hybridized to a probe location." (D.I. 240 at 32.) The dispute here is whether the Court should construe "probe intensity" to require that the intensity come from a labeled sample nucleic acid and that the intensity be associated with a particular probe location. The Court concludes that Illumina's construction is appropriate.

Affymetrix contends that there are many ways to generate a signal indicating the extent of hybridization other than by labeling the sample sequence that hybridizes to a probe. (D.I. 243 at 32.) While not disputing that all of the embodiments and examples in the '716 patent's specification describe "probe intensities" as coming from labeled sample nucleic acids, Affymetrix argues that imposing such a limitation on the claims would be an improper importation from the specification. (Id. at 33.) However, this is not a case of improperly importing a limitation from the specification into the claims, but of reading a claim in light of the specification. See Phillips,

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415 F.3d at 1323 (stating that "there is sometimes a fine line between reading a claim in light of the specification and reading a limitation into the claim from the specification"). It may be true, as Affymetrix argues, that there are other methods of generating signals indicating the extent of hybridization. It is clear, however, from the specification's consistent descriptions of "probe intensities" as arising from labeled sample sequences, and its lack of discussion of any alternative method, that "what the inventors actually invented and intended to envelop with [their claims]," Phillips, 415 F.3d at 1316, is a system in which "probe intensities" are generated by labeled sample nucleic acids hybridized to probes.

Similarly, all of the embodiments and examples in the specification indicate that the "probe intensities" must be associated with known probe locations. Moreover, during patent prosecution, the inventors clearly and unmistakably limited the scope of their claims to require that the location of the hybridized probes be known. (See D.I. 244, Ex. DD at 14 (distinguishing prior art references on the grounds that "[i]n the present invention, the locations of the hybridized probes are known . . . .").) Therefore, the Court construes "probe intensity" to mean "intensity from a labeled sample nucleic acid hybridized to a probe location."

3.   Construction Of "Corresponding To Probe
     Intensities For A Plurality Of Nucleic Acid
     Probes"

Affymetrix's proposed construction of "corresponding to

probe intensities for a plurality of nucleic acid probes" is

"relating to a detectable signal, e.g. fluorescence, from two or

more nucleic acid sequences of known sequence that are capable

of hybridizing to a complementary sequence." (D.I. 243 at 34.)

Illumina's proposed construction is "two or more probe locations

each having one and only one probe intensity." (D.I. 240 at

34.)   The Court has construed "probe intensity" and "probe," and

the meaning of "plurality" is not in dispute.   Therefore, the

dispute here is over the meaning of the term "corresponding."

In essence, Illumina contends that "corresponding" requires a

one-to-one correspondence between the signals and the probes.

That is, for each probe, there must be one and only one

intensity, and thus, one and only one signal.   (D.I. 240 at 34.)

The Court disagrees.

The language of claim 1 does not require such a limitation.

Indeed the language "each probe intensity indicating an extent

of hybridization of a nucleic acid probe with at least one

nucleic acid sequence . . . ,"   ('716 patent, col. 41,ll. 65-67

(emphasis added)), indicates that the inventors contemplated

embodiments in which a nucleic acid probe would be hybridized

with more than one nucleic acid sequence.   In such a case, a

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single probe would have more than one intensity associated with
it, one for each labeled sequence with which it was hybridized.
Moreover, this sort of process is explicitly claimed in claims
3, 4, 7, and 8, in which the probes are hybridized with both a
reference sequence and a sample sequence.

The Court has construed "probe intensity" and "probe," and
has concluded that a limitation on "corresponding" is not
required. Therefore, the Court concludes that no further
construction of the term "corresponding to probe intensities for
a plurality of nucleic acid probes" is necessary.

> 4.   Construction of "Indicating An Extent Of
>   Hybridization"

Affymetrix's construction of "indicating an extent of
hybridization" is "relating to the relative binding of." (D.I.
243 at 35.) Illumina's proposed construction is "indicating the
strength of binding so as to distinguish a single-base
mismatch." (D.I. 240 at 35.) The proposed constructions of
both parties construe "hybridization" as "binding." Both
parties also agree that "extent of hybridization" refers to the
relative strength or amount of binding. (D.I. 243 at 35; D.I.
240 at 35.) The dispute here, then, concerns Illumina's proposed
addition of the limitation "so as to distinguish a single-base
mismatch." The Court concludes that such a limitation is not
required.

Claim 1 requires that the nucleic acid probes "differ[]

from each other by <u>at least</u> a single base . . . ."   ('716
patent, col. 42, ll. 59-60 (emphasis added).)   The use of the
language "at least" indicates that the inventors contemplated
embodiments in which the probes differ from each other by more
than a single base.   In such embodiments the limitation "so as
to distinguish a single-base mismatch" would be wholly
misplaced.   Therefore, the Court construes "indicating an extent
of hybridization" to mean "indicating the relative strength of
binding."

     5.   <u>Construction Of "Comparison Of Said Plurality Of
Probe Intensities To Each Other"</u>

Affymetrix's proposed construction of "comparison of said
plurality of probe intensities to each other" is "an examination
of the detectable signals of two or more probes in relation to
each other."   (D.I. 243 at 36.)   Illumina's proposed
construction is "ranking of probe intensities from a
hybridization experiment."   (D.I. 240 at 36.)   The dispute here
is whether the "comparison" must be a "ranking."   The Court
concludes that the "comparison" need not be a ranking.

The specification teaches several methods of comparison
including the Intensity Ratio Method ('716 patent, col. 7, l. 34
- col. 10, l. 39), the Reference Method (<u>Id.</u>, col. 10, l. 40 -
col. 17, l. 44), and the Statistical Method (<u>Id.</u>, col. 17, l. 45
- col. 22, l. 34).   None of these methods can accurately be
characterized as simply a "ranking of probe intensities."   Thus,

Illumina's proposed construction would exclude these
embodiments. A proposed construction that excludes an
embodiment "is rarely, if ever, correct and would require highly
persuasive evidentiary support. . . ." Vitronics, 90 F.3d at
1583. The Court finds no such support here. Therefore, the
Court construes "a comparison of said plurality of probe
intensities to each other" to mean "an examination of the probe
intensities of two or more probes in relation to each other."

> 6. Construction Of "Generates A Base Call Identifying
>   Said Unknown Base"

Affymetrix's proposed construction of "generates a base
call identifying said unknown base" is "determines which
nucleotide is most likely to be present at a particular position
in a nucleic acid sequence." (D.I. 243 at 37.) Illumina's
proposed construction is "identifies a nucleotide as A, C, G or
T(or U)." (D.I. 240 at 38.) The dispute here is over the
specificity with which a nucleotide must be identified. The
Court concludes that Affymetrix's proposed construction is more
accurate.

As described in the specification, the invention does not
necessarily call bases by identifying an unknown base as simply
A, C, T, or G(or U). While it may call a base as a specific
nucleotide, it may also call it "as being ambiguously one of two
or more bases . . . ." ('716 patent, col. 9, ll. 22-25; see

also <u>Id.</u>, col. 8, ll. 8-30 (listing the various codes that may be assigned to bases by a base call).)   Therefore, the Court construes "generates a base call identifying said unknown base" to mean "determines which nucleotide is most likely to be present at a particular position in a nucleic acid sequence."

> 7. <u>Construction Of "Generates A Base Call . . .
> According To Results Of Said Comparison And Said
> Sequences Of Said Nucleic Acid Probes"</u>

Affymetrix's contends that this phrase does not need further construction because it is a "collection of several of the phrases and terms already construed."   (D.I. 243 at 39). Illumina proposes the construction "generates a base call as the base-pair complement to the probe with the highest probe intensity(ies)."   (D.I. 240 at 38).   The Court agrees with Affymetrix.   The Court has construed the significant terms and phrase within this phrase, i.e. "generates a base call," "said comparison," and "said nucleic acid probes."   Therefore, no further construction is required.

<div align="center">CONCLUSION</div>

An Order consistent with this Memorandum Opinion will be entered setting forth the meaning of the disputed terms and phrases in the patents-in-suit.